

Prevention of Growth Failure in Turner Syndrome: Long-term Results of Early Growth Hormone Treatment in the “Toddler Turner” Cohort

-- Supplemental Material--

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1. Statistical methods for primary analysis

For the original randomized Toddler Turner trial the protocol-defined sample size estimate required 72 protocol-completing subjects (36 per group) and a between-group height difference of at least 0.5 standard deviation score (SDS) at the end of the 2-year study to provide 80% power for a one-tailed t-test at a significance level of 0.05 [35]. The large treatment effect at the end of the primary study (1.6 SDS between-group height difference, with 78 protocol-completing subjects) provided ample power to support the original hypothesis. However, for the Extension study it was assumed that between-group differences would diminish with time because untreated control subjects would transition to treatment, making it challenging to examine the effect many years later of the original 2 years of GH in the Early-Treated group, or to anticipate its direction, leading us to select a 2-sided analysis. Because the number of Toddler study participants who would enroll in the Extension was unknown, various estimates of statistical power were examined *a priori*, based on

hypothetical combinations of potential subject numbers and between-group height SDS differences at near-adult height (NAH). For example, to achieve 80% power in a 2-sided, 2-sample t-test would require 43 subjects per group (i.e., 86 of the original 88 Toddler study participants) and a between-group height difference at NAH of 0.75 SDS (i.e., greater than the *a priori* estimate for the original randomized Toddler study); fewer subjects available at NAH would require an even greater height difference.

2. Statistical methods for Quantitative Insulin Sensitivity Check Index (QUICKI)

Insulin sensitivity was estimated using the quantitative insulin sensitivity check index (QUICKI: $1/[\log(I_0) + \log(G_0)]$, where I_0 is fasting insulin and G_0 is fasting glucose) [Reference: Hrebicek J, Janout V, Malincikova J, Horakova D, Cizek L: Detection of insulin resistance by simple quantitative insulin sensitivity check index QUICKI for epidemiological assessment and prevention. J Clin Endocrinol Metab 2002; 87:144-147].

3. Supplemental Table: Demographic data for subjects from Toddler study who did not participate in Extension study

	Early Treated n = 9	Early Untreated n = 11 ¹	P value ²	Overall n = 20
Age at Toddler study baseline, yr	2.15 ± 1.19	2.16 ± 1.06	0.98	2.16 ± 1.09
Height SDS at Toddler study baseline	-1.65 ± 0.51	-2.15 ± 1.03	0.20	-1.93 ± 0.86
Age at Toddler study endpoint, yr	3.90 ± 1.40	3.71 ± 1.31	0.76	3.80 ± 1.32
Height SDS at Toddler study endpoint ³	-1.08 ± 0.63, n=6	-2.57 ± 1.33, n=8	0.03	-1.93 ± 1.33, n=14

Data are mean ± SD.

¹Includes one subject who was ineligible for the Extension study because of 46,XX karyotype discovered after entry to the Toddler study.

²P values are for comparison of means between ET and EUT groups by ANOVA.

³Lower subject numbers due to departure prior to completion of Toddler study for 6 of 20 subjects